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[54] **VECTORS HAVING ENHANCED EXPRESSION, AND METHODS OF MAKING AND USES THEREOF**

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[58] **Field of Search** 514/44; 424/93.2; 435/69.1, 172.3, 320.1

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,738,922	4/1988	Haseltine et al.	435/69.3
5,302,517	4/1994	Rhode, III	435/69.1

OTHER PUBLICATIONS

Park et al., Proc. Natl. Acad. Sci. USA 91:4713–4717 (1994).

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[57] **ABSTRACT**

Disclosed and claimed are vectors having enhanced expression and methods for making and using them. Enhancement of expression is from substantially co-temporal expression of at least one first nucleic acid molecule and at least one second nucleic acid molecule. The second nucleic acid molecule encodes a transcription factor or a translation factor or a transcription factor and a translation factor. The contemporaneous expression can be from operably linking the first and second nucleic molecules to a single promoter, or from operably linking the first nucleic acid molecule to a first promoter and the second nucleic molecule to a second promoter wherein the first and second promoters function substantially contemporaneously. Thus, the first and second nucleic acid molecules can be at the same locus in the vector, or at different loci. The second nucleic acid molecule can encode: one transcription factor or more than one transcription factor; or one translation factor or more than one translation factor; or at least one transcription factor and at least one translation factor. The transcription factor can be from vaccinia H4L, D6, A7, G8R, A1L, A2L, H5R, or combinations thereof. The translation factor can be from a K3L open reading frame, an E3L open reading frame, a VAI RNA, an EBER RNA, a sigma 3 open reading frame, a TRBP open reading frame, or combinations thereof. The vector can be a poxvirus such as an attenuated poxvirus, e.g., NYVAC, or ALVAC.

51 Claims, 30 Drawing Sheets